201-14667

NCIC HPV
Sent by: Mary-Beth Weaver

08/14/2003 02:29 PM

To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on 4-Nitrophenol (CAS# 100-02-7)

Richard_Denison@environmentaldefense.org on 08/14/2003 09:44:42 AM

To: oppt.ncic@epamail.epa.gov, hpv.chemrtk@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, frjoha@solutia.com
cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org

Subject: Environmental Defense comments on 4-Nitrophenol (CAS# 100-02-7)

(Submitted via Internet 8/14/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and frjoha@solutia.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 4-Nitrophenol (CAS# 100-02-7).

The test plan and robust summaries for 4-nitrophenol (NP), also termed p-nitrophenol, was submitted by Solutia, Inc. NP is apparently manufactured by the sponsor at a single site and sold to customers at other sites for the purpose of full chemical conversion into other industrial chemicals. However, use practices of the customers are not monitored, so it may have other applications not reported in this test plan.

NP possesses high acute toxicity and can cause methemoglobinemia in workers. The sponsor states that practices are in place to minimize worker exposure, but they are not detailed nor is their any information presented on maximum allowable concentrations in the workplace. Likewise, no data are provided on environmental releases. If NP is synthesized in a closed system, as the sponsor maintains but does not document in the test plan, any releases during production should be minimal. Transport (including export) and conversion as a chemical intermediate are mentioned but potential releases from such activities are not characterized in the test plan.

The test plan is well-written and organized and the sponsor claims that no new studies are needed to fulfill HPV requirements. We agree with this claim with one exception. Based on the information presented in the robust summaries, a developmental toxicity study needs to be conducted. Specific comments are provided below:

1. Existing studies on environmental fate and distribution and ecotoxicity studies are adequate for screening level purposes. The sponsor states that although NP is resistant to hydrolysis, it should not bioaccumulate in aquatic organisms. We agree with the sponsor for the reasons stated in the test plan. We also note that NP is rapidly conjugated by most organisms and this process renders the molecule non-toxic and water-soluble.

2. Acute toxicity studies using multiple routes of exposure indicate that NP is toxic when administered orally or via inhalation. In contrast, it is not acutely toxic when administered dermally.

3. Existing repeat dose studies are more than adequate to fulfill HPV requirements, as there are multiple studies in multiple species. These studies also indicate that NP is toxic via the inhalation and oral routes

RECEIVED
OPPT CBIC
2003 AUG 14 PM 3:09

but not the dermal route.

4. There are substantial studies which have examined the in vitro genetic toxicity of NP, but no in vivo studies -- although there are in vitro studies on chromosomal aberrations in CHO cells. Taken together, we agree with the sponsor that in vivo genetic toxicity studies on NP are not necessary.

5. The robust summary contains only a 2-generation reproductive study on NP administered via the dermal route. No developmental toxicity studies were reported. Since dermally-administered NP is not acutely toxic and no information was provided on the systemic levels of NP following dermal administration, the reproductive/ developmental dataset is inadequate for screening level purposes. We do note that no histological alterations of reproductive organs were detected in the oral or inhalation repeat dose studies, so a new reproductive toxicity study is not needed. However, an oral or inhalation developmental toxicity study is warranted, as data on this endpoint are not available.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Richard Denison, Ph.D.
Senior Scientist, Environmental Defense